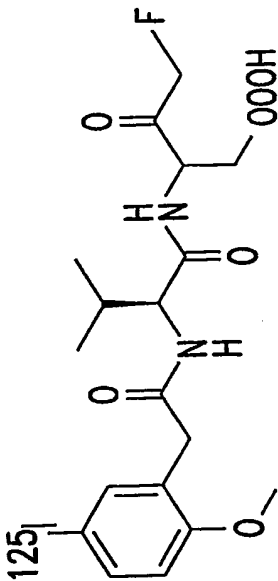


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k_{inact} (S^{-1})
CASPASE-1 7.0 X 10^{-6}
CASPASE-3 1.6 X 10^{-5}
CASPASE-7 1.2 X 10^{-6}
CASPASE-8 3.7 X 10^{-5}



[¹²⁵I]-M808

FIG.1

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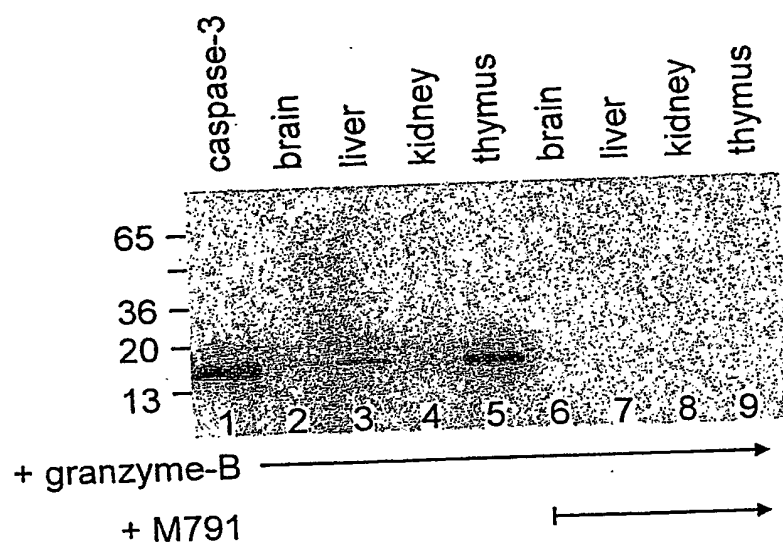


FIG.2A

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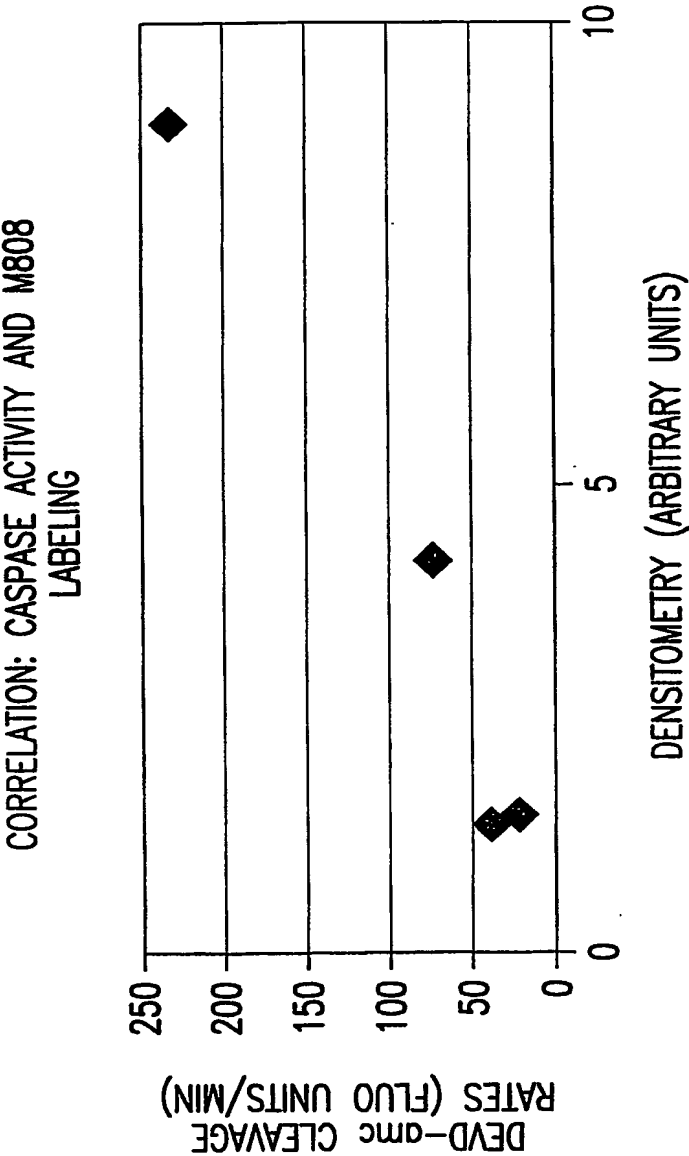


FIG.2B

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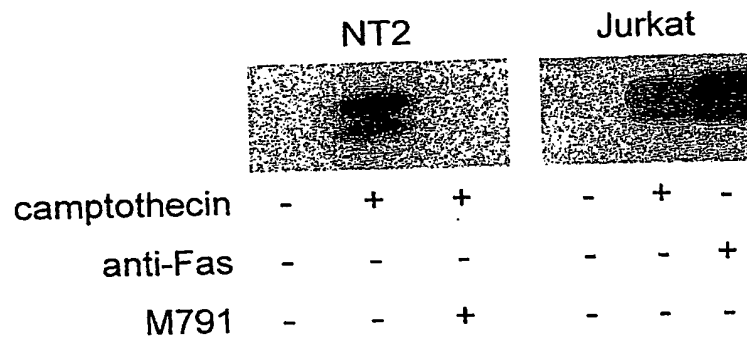


FIG.2C

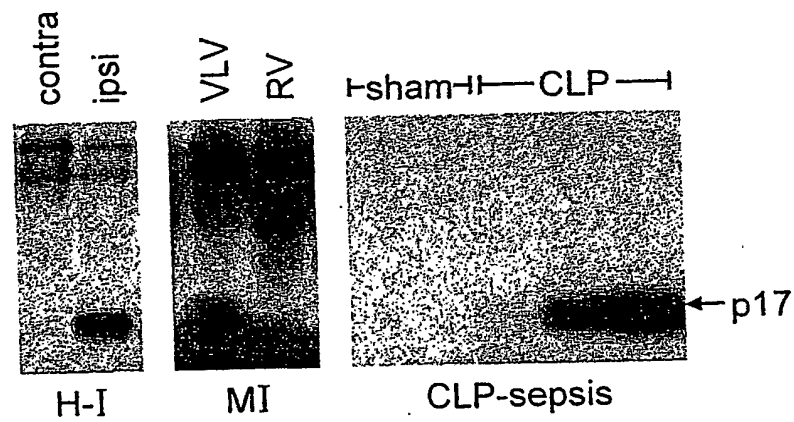


FIG.2D

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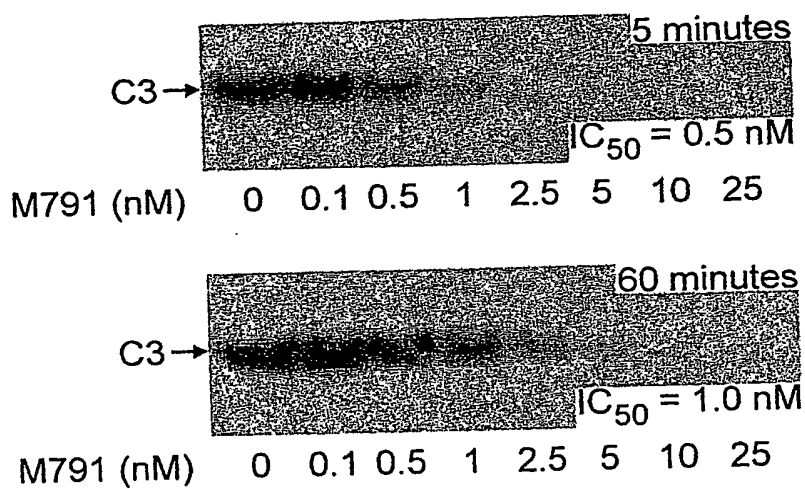


FIG.3A

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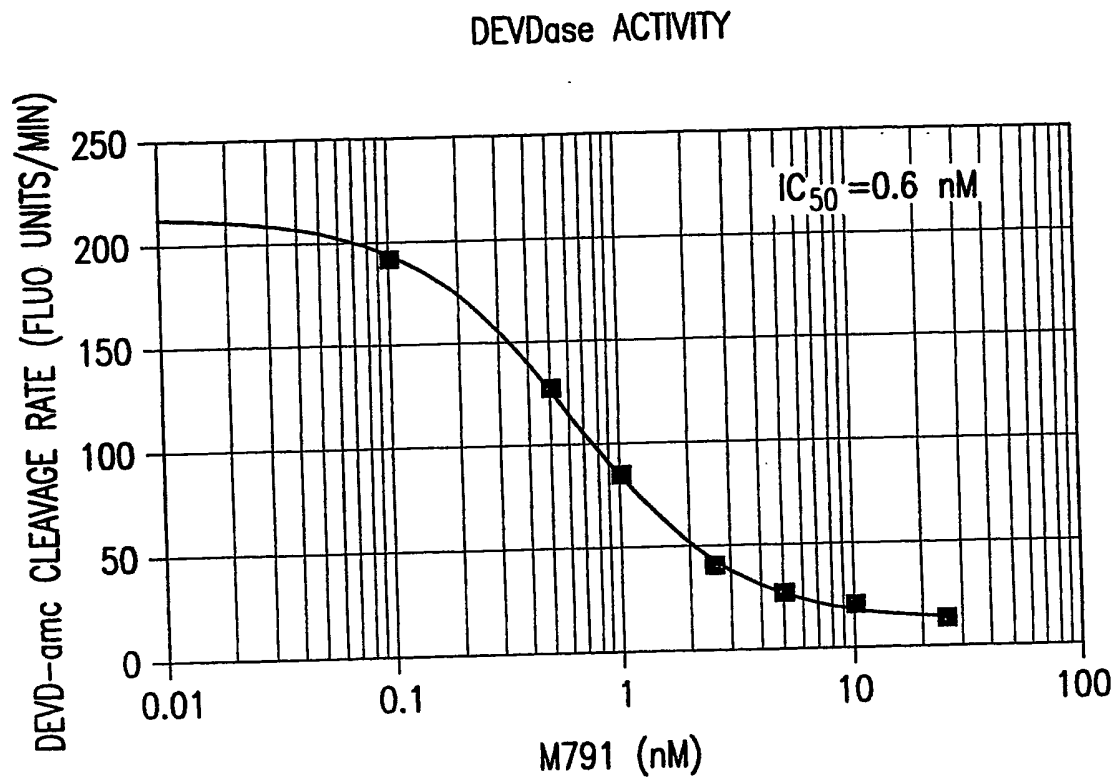


FIG.3B

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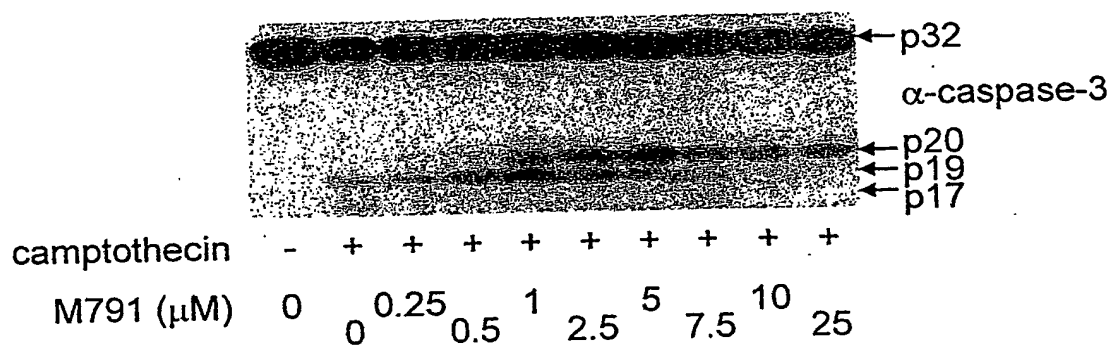


FIG.4A

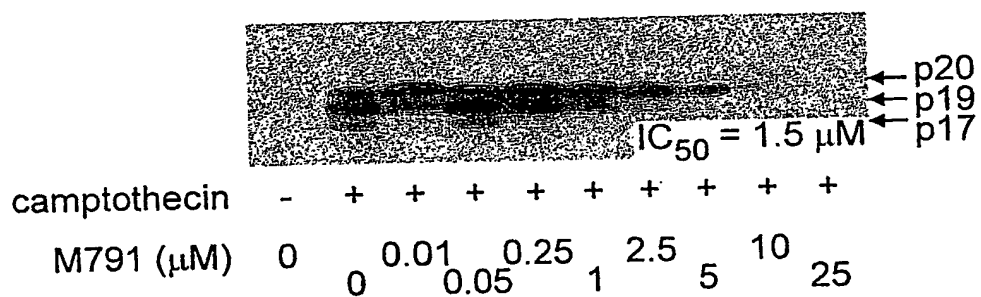


FIG.4B

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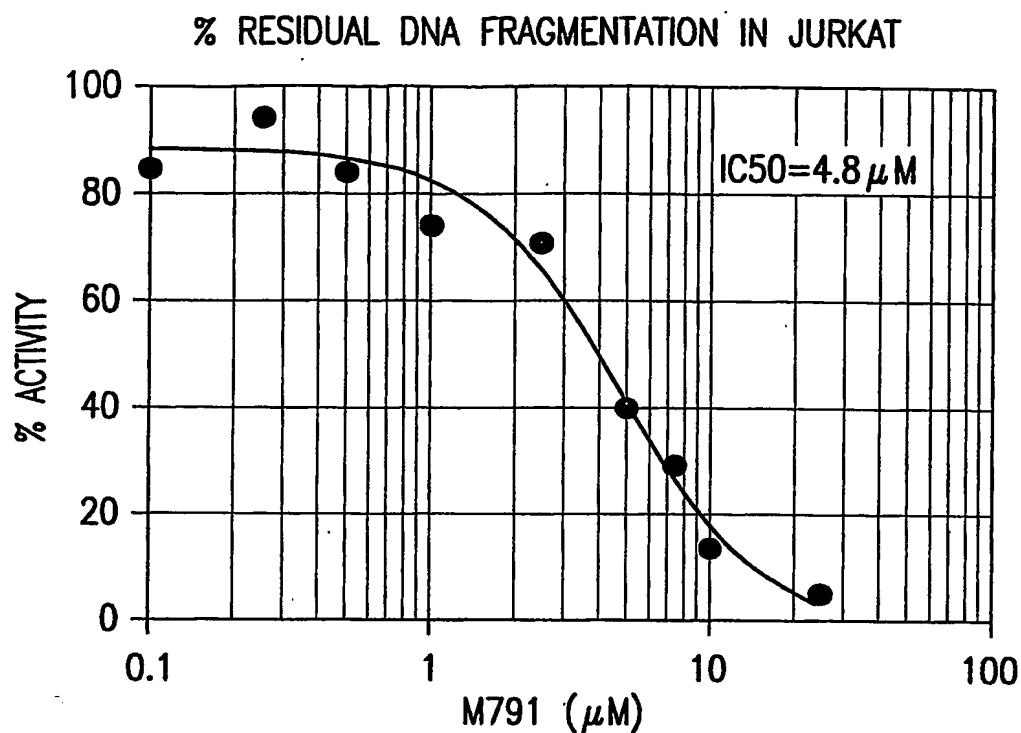


TABLE II. COMPARATIVE POTENCIES OF CASPASE INHIBITORS MEASURED BY M808 AND DNA FRAGMENTATION

CELL LINE	INHIBITOR	IC50 PROBE (μM)	IC50 DNA CLEAVAGE (μM)
NT2	M791	0.5	0.4
NT2	M826	0.045	0.03
NT2	M090	3.6	7
JURKAT	M791	2.5	4.8
JURKAT	M826	0.045	TO BE DETERMINED
THYMOCYTES	M826	0.07	0.14
THYMOCYTES	M867	0.09	0.27

FIG.4C

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- DETERMINE EXPECTED [¹²⁵I]-M808 SIGNAL IN DRUG-TREATED ANIMAL, BASED ON MEASURED TOTAL AMOUNT OF CASPASE-3, AS MEASURED BY WESTERN BLOT
- EXPECTED [¹²⁵I]-M808 SIGNAL: 3.6 UNITS
- ACTUAL [¹²⁵I]-M808 MEASURE: 1.0 UNIT
- FREE ENZYME = ACTUAL/EXPECTED
= 1.0 UNITS/3.6 UNITS = 0.28
= 28% FREE CASPASE ACTIVE SITES

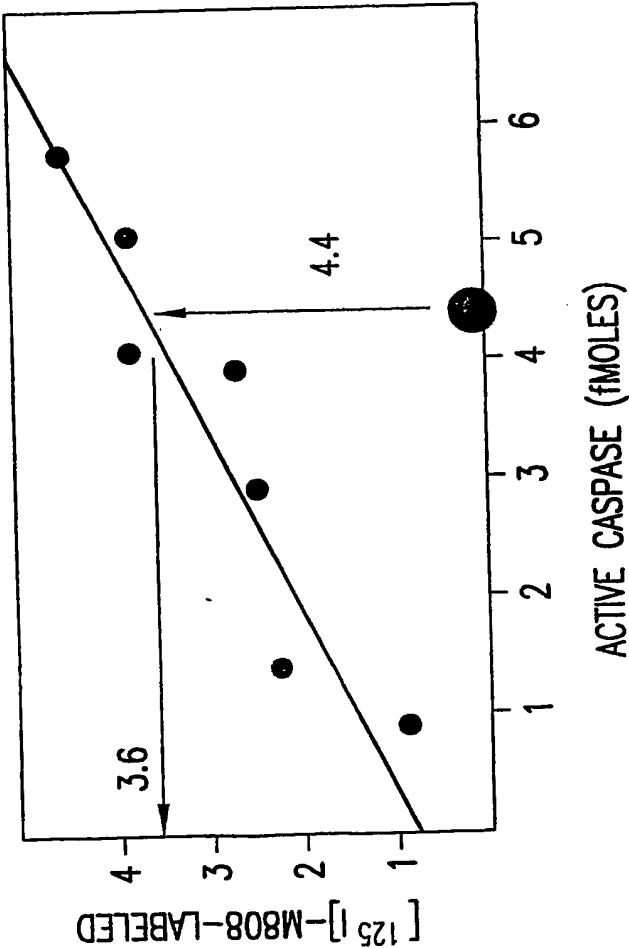


FIG.5A

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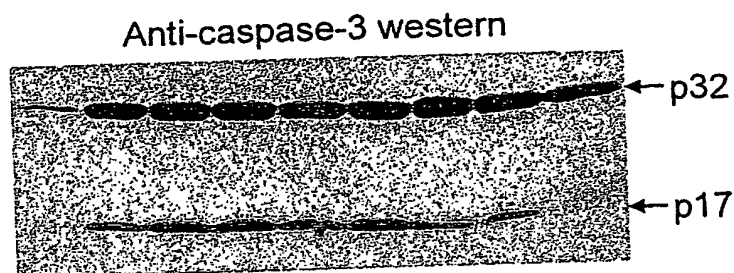


FIG.5B

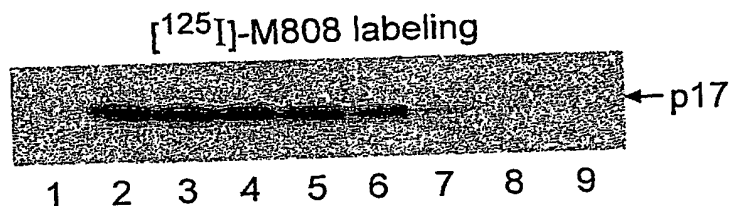


TABLE III. PERCENT OCCUPANCY OF CASPASE ACTIVE SITE BY M867 IN APOPTOTIC RAT THYMOCYTES									
LANE	1	2	3	4	5	6	7	8	9
M867 CONCENTRATION (μM)	0	0	0.005	0.025	0.05	0.1	0.25	1	5
p17 DENSITOMETRY	0.6	14.3	17.6	19.0	17.1	19.2	11.3	10.2	4.6
EXPECTED ^{125}I M808 SIGNAL*			52.7	56.9	51.4	57.6	34.0	30.6	13.9
ACTUAL ^{125}I M808 SIGNAL	4.7	42.6	42.8	40.4	39.1	28.4	11.9	3.7	0.0
RATIO ACTUAL/EXPECTED			0.8	0.7	0.8	0.5	0.4	0.1	0.0
% FREE ACTIVE SITES			81	71	76	49	35	12	0
% OCCUPANCY			19	29	24	51	65	88	100

* EXPECTED $[^{125}\text{I}]$ M808 SIGNAL CALCULATED BASED ON p17 DENSITOMETRY vs $[^{125}\text{I}]$ -M808 SIGNAL IN ABSENCE OF DRUG

FIG.5C

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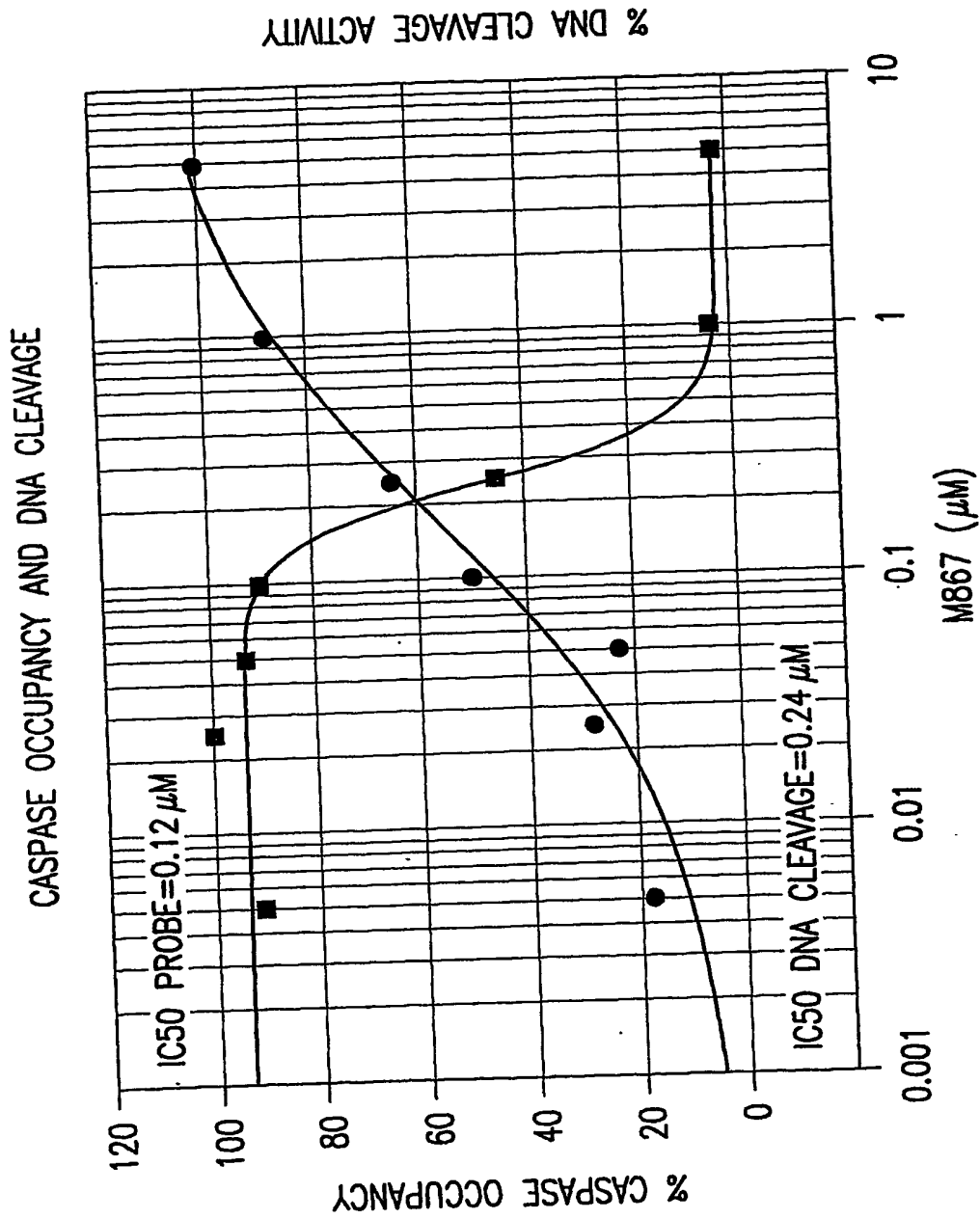


FIG.5D

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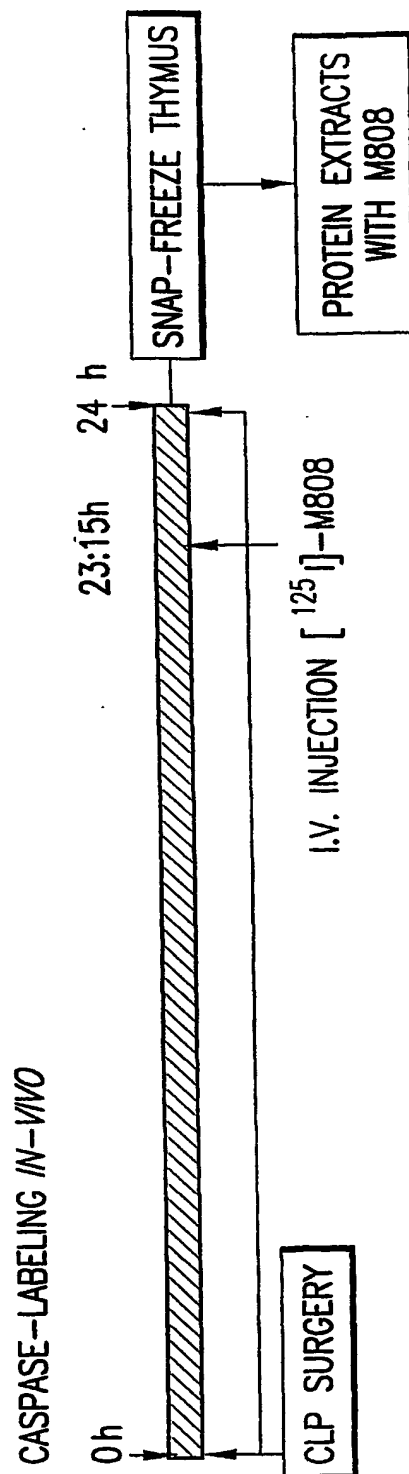


FIG. 6A

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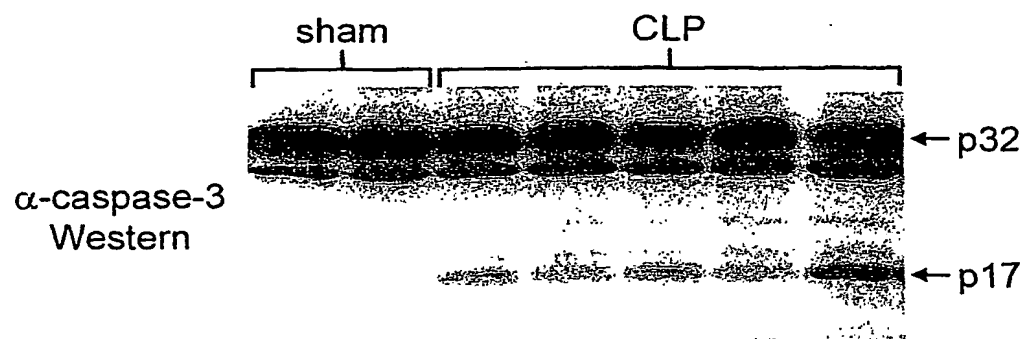


FIG.6B

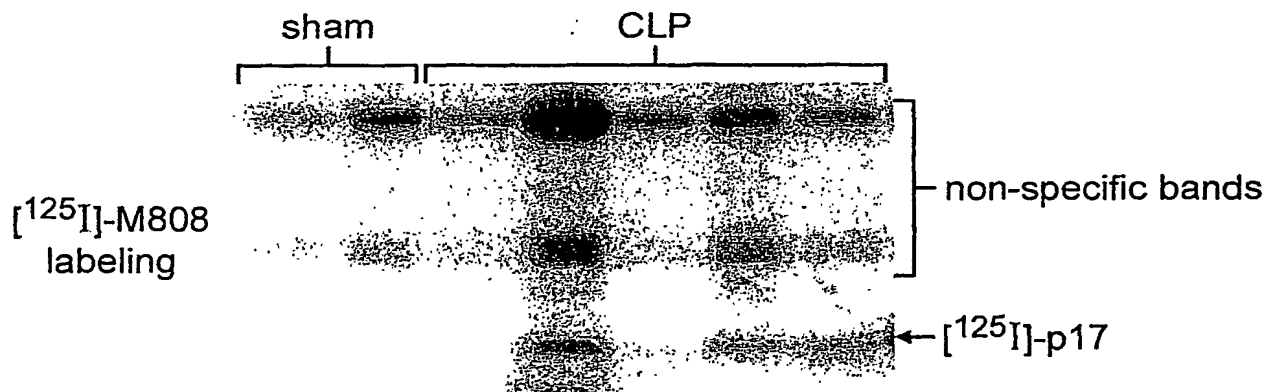


FIG.6C

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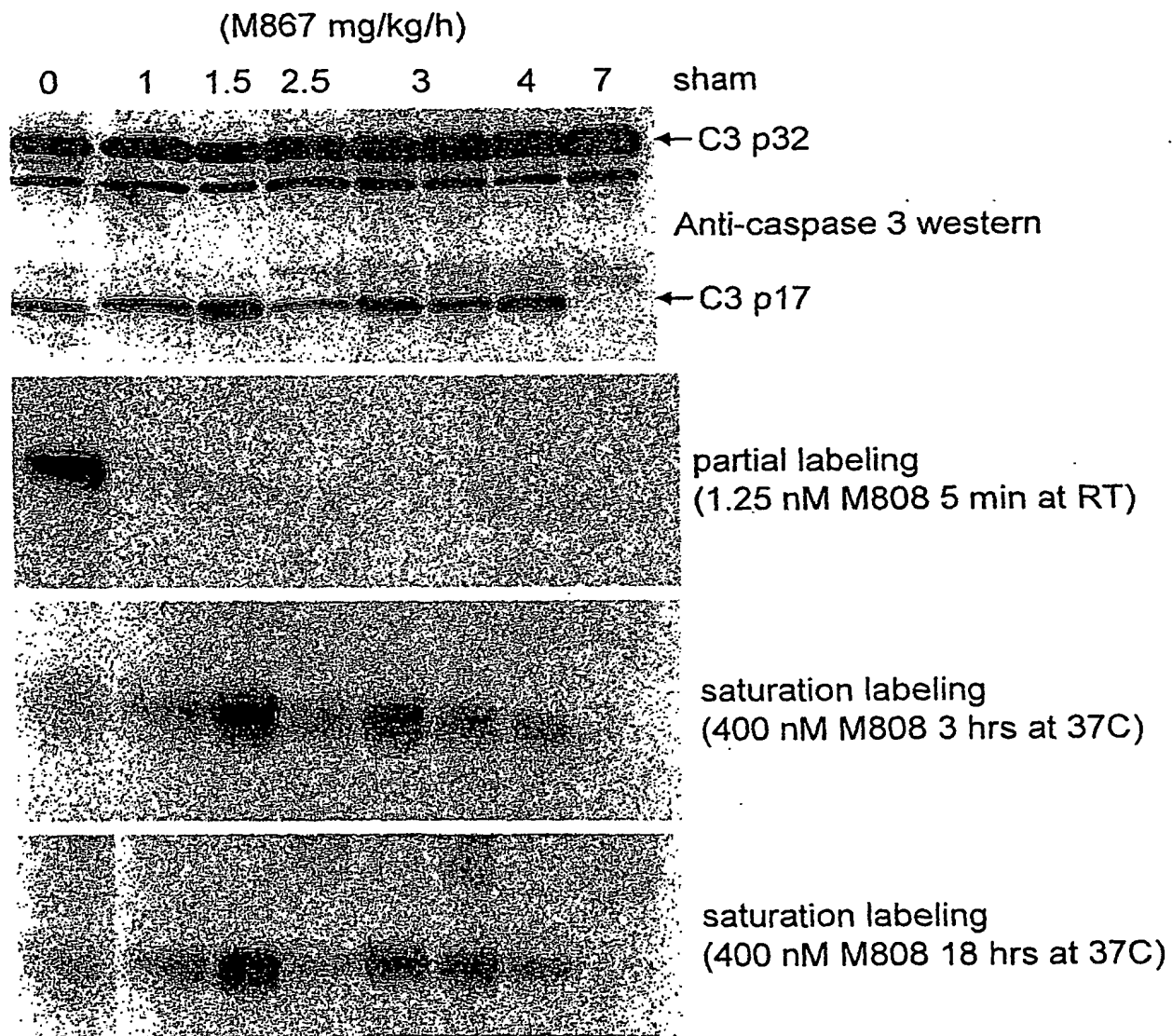


FIG.7

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